

BIOGRAPHICAL SKETCH

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NAME THEOHARIDES, THEOHARIS C.	POSITION TITLE Professor of Pharmacology and Internal Medicine (Allergy & Clinical Immunology)		
eRA COMMONS USR NAME (credential, e.g. agency login) THEOHAR			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Yale University, New Haven, CT	B.A.	1972	Biology & Hist. Medicine
Yale University, New Haven, CT	M.S.	1975	Neuroimmunology
Yale University, New Haven, CT	M.Phil.	1975	Immunopharmacology
Yale University, New Haven, CT	Ph.D.*	1978	Pharmacology
Yale University, New Haven, CT	M.D.	1983	Medicine
Tufts University, Fletcher School Law & Diplomacy	Certificate	1999	Leadership & Management
Harvard Univ, J.F. Kennedy School of Government	M.P.A.	Deferred	Biomedical Res Policy

*Doctoral Thesis advisors: W.W. Douglas, M.D.-Royal Acad. Sciences; Paul Greengard, Ph.D.-2000 Nobel Laureate in Physiol & Med; Doctoral Thesis examiner, George E. Palade, M.D.- 1974 Nobel Laureate in Physiology & Medicine

A. Personal Statement

I have been studying the regulation of mast cell activation and its role in neuroinflammatory diseases for over 20 years. I was the first to report that mast cells: (a) can secrete specific mediators selectively without degranulation, that (b) can regulate blood-brain-barrier permeability, (c) can be activated by corticotropin-releasing hormone (CRH) to release VEGF selectively, (d) can be activated by synergistic action of CRH and neurotensin under stress, (e) can be activated by IL-33 and substance P synergistically, and (f) can secrete prestored TNF, accompanied by mitochondrial fission, translocation to the cell surface and release of mitochondrial DNA. I have been placed in the top 1% of authors most cited in pharmacological and in the top 5% of immunological journals.

B. Positions and Honors

1968-1971 Assistant in Research, Department of Biology, Yale University, New Haven, CT
 1971-1978 Assistant in Research, Department of Pharmacology, Yale University, New Haven, C
 1978-1983 Research Associate, Allergy & Clin. Immunology, Dept. Internal Med, Yale
 1984-1986 Associate in Clinical Immunology, Tufts University School of Medicine, Boston, MA
 1986-1993 Training in Internal Medicine, Dept. of Internal Medicine, NEMC, Center, Boston,
 1985-1992 Director of Medical Pharmacology, Tufts University School of Medicine, Boston,
 1983-1988 Assistant Professor of Pharmacology, Biochemistry and Psychiatry, Tufts University
 1989- Associate Professor of Pharmacology (1989-1994), Biochemistry and Psychiatry, Tufts
 1995- Professor of Pharmacology, and Biochemistry (2002-), Tufts U (tenured 11/2/91)
 1995- Professor of Internal Medicine (Allergy Section), Tufts Univ & Tufts Medical Center
 2004- Director, Molecular Immunopharmacology and Drug Discovery Laboratory, Tufts

Honors

1971 *Connecticut Commission for Undergraduate Research Award*
 1971 *Yale College Dean's Award* for senior research thesis
 1972 *Cum Laude & Divisional Honors* for joint Bachelor of Arts, Yale College
 1972 *Theodore Cuyler Award* "for outstanding Yale College graduates," Yale University
 1975-1977 *Advisory Committee to the Dean, Yale University Graduate School*
 1977 *G. Papanicolaou Graduate Research Award*, Hellenic University Club of New York
 1979-1983 *Medical Award*, Hellenic Medical Society of New York
 1980 *Winternitz Prize* "for the best work in Pathology," Yale Univ. School of Medicine

1981-1982 *Research Fellowship*, International Inst. of Cellular & Molecular Pathology, Brussels
 1986-1989 *Chairman - Neuroimmunology*, 2nd & 3rd World Conf on Inflammation, Monte Carlo
 1986 *Distinguished Service Citation* for faculty excellence, Tufts University
 1987-1988 *Special Faculty Recognition Award*, Tufts University School of Medicine
 1987 *Member, Alpha Omega Alpha National Medical Honor Fraternity*, USA
 1989-1996 *Citation for Excellence in Teaching*, Tufts University School of Medicine
 1993 *Medical Awareness and Patient Support Award*, Interstitial Cystitis Association, NY
 1994 *Diocesan Award for Humanitarian Health Care*, Greek Orthodox Diocese of Boston
 1995 *Chairman*, International Committee to Upgrade Medical Education in Greece
 1997-2001 *Supreme Scientific Advisory Health Council*, Secretary of Health, Hellenic Republic
 1998 *Community Service Award*, Mayor Thomas Menino of Boston, MA
 1999-2002 *Supreme Health Board*, Instit of Social Welfare, Sec. of Labor & Human Res,
 1999 *Oliver Smith Award* "recognizing excellence, compassion and service", NEMC
 1999 *Archon of the Ecumenical Patriarchate of Constantinople*, Greek Orthodox Church
 2002 *Dr. George Papanicolaou Gold Medal* for contributions in humanism and medicine
 2003-2008 *National Public Health Council*, Secretary of Health, Hellenic Republic
 2006 *Hygeia Award*, New Engl. Hellenic Medical & Dental Society, Boston, MA
 2007 *Science and Medicine Award*, Fed. HASNE, Boston, MA
 2008 *Fellow*, American Academy of Allergy, Asthma, Immunology
 2009 *Fellow*, European Academy of Allergology and Clinical Immunology
 2011 *Honorary Doctor of Medicine*, Athens University (conferred January, 2011)
 2013 *Honorary Doctor of Science*, HellenicAmerican University (conferred October, 2013)

Public Advisory Committees

1986-2018 Massachusetts Drug Formulary Commission
 2001-2002 NSF Div. Integrative Biology and Neuroscience
 2000-2002 NIH Biobehavioral & Behavioral Processes-SS2
 2002 NIH ZDK1 GRB-B (J2) Biol Neuroendoc Peptides
 2002 NIH ZDK11 GRB-9 Urology Research Centers
 2002 NIDDK Reparative Medicine Section (SSS-M)
 2003 VA Neurobiology Section A
 2004 Italian Ministry of Universities and Research
 2007 ZAI1 SV-IS1 Cellular & Inflammatory Pathways
 2007 NIAID Asthma & Allergic Diseases Cooperative Research Centers
 2008 NIH ZRG1 CFS-D
 2009 NIH ZDK1 GRB-6 Urology Research Centers
 2009 SEP, National Center for Minority Health & Disparities (NCMHD)
 2010 NIMSD ZRG1 MOSS-D12B SBIR: Dermatology, Rheumatology and Inflammation
 2012 ZRG1 CFS-M (80) S-Chronic Fatigue Syndrome
 2012 ZRG1 MOSS T12- Small Business: Dermatology, Rheumatology and Inflammation
 2012 ZRG1 MOSS-S (04) S-Musculoskeletal, Oral a& Skin Sciences
 2013 ZRG1 VH-D 02M Molecular and Cellular Hematology
 2015 ZRG1 MOSS-V (02) M Special Emphasis Panel
 2015 ZRG1 MOSS-C (02) Skin Immunology-CHAIR
 2016 ZRG1 MOSS-C (02) Skin Immunology

Patents

Methods: US No. 5,250,529; 5,648,350; 5,821,259; 5,855,884; 5,994,357; 6,020,305; 6,689,748; 7,759,307;
 7,923,0431; 8,268,365; 9,050,275; 12/534,571 (Allowed). EPO No. 0618796; EPO No. 0748217

Compositions: US No. 6,624,148; 6,635,625; 6,641,806; 6,645,482; 6,984,667; 7,155,278; 7,906,153; 7,799,766

C. Contribution to Science (publications selected from 382 in Pubmed.gov; 23,510 citations; h-index 73).

1. Mast cells secrete the mediators selectively, thus participating in different biological processes.

- Sieghart W, Theoharides TC, Alper LS, Douglas WW, Greengard P. Calcium dependent protein phosphorylation during exocytotic release of mast cell secretory granules. *Nature* 1978; 275:329-331. PMID: 357989

- Theoharides TC, Douglas WW. Secretion in mast cells induced by calcium entrapped within phospholipid vesicles. **Science** 1978; 201:1143-1145. PMID: 684435
- Theoharides TC, Sieghart W, Greengard P, Douglas, WW. Anti-allergic drug cromolyn may inhibit histamine secretion by regulating phosphorylation of a mast cell protein. **Science** 1980; 207:80-82. PMID: 6153130
- Theoharides TC, Bondy PK, Tsakalos ND, Askenase PW. Differential release of serotonin and histamine from mast cells. **Nature** 1982; 297:229-231. PMID: 6176873
- Kandere-Grzybowska K, Letourneau R, Kempuraj D, Donelan J, Poplawski S, Boucher W, Athanassiou A, Theoharides TC. L-1 induces vesicular secretion of IL-6 without degranulation from human mast cells. **J Immunol.** 2003; 171(9):4830-6. PMID:14568962

2. ***Stress has pro-inflammatory effects through CRH-induced mast cell activation.***

- Esposito P, Chandler N, Kandere K, Basu S, Jacobson S, Connolly R, Tutor D, Theoharides TC. Corticotropin-releasing hormone and brain mast cells regulate blood-brain-barrier permeability induced by acute stress. **J Pharmacol Exp Ther.** 2002; 303(3):1061-6. PMID: 12438528
- Cao J, Papadopoulou N, Kempuraj D, Boucher WS, Sugimoto K, Cetrulo CL, Theoharides TC. Human mast cells express corticotropin-releasing hormone (CRH) receptors and CRH leads to selective secretion of vascular endothelial growth factor (VEGF). **J Immunol.** 2005; 174:7665-7675. PMID: 15944267
- Donelan J, Papadopoulou N, Marchand J, Kempuraj D, Lytinas M, Boucher W, Papaliodis D, Theoharides TC. Corticotropin-releasing hormone (CRH) induces skin vascular permeability through a neurotensin (NT)-dependent process. **Proc Natl Acad Sci USA.** 2006; 103:7759-7764. PMID: 16682628; [PMCID: 2840132](#)
- Vasiadi M, Therianou A, Sideri K, Smyrnioti M, Delivani D, Sismanopoulos N, Asadi S, Katsarou-Katsari A, Petrakopoulou D, Theoharides A, Antoniou C, Stavrianeas N, Kalogeromitros D, Theoharides TC. Increased serum CRH levels with decreased skin CRH-R1 gene expression in psoriasis and atopic dermatitis. **J Allergy Clin Immunol.** 2012; 129(5):1410-3. PMID: 22360979; [PMCID: PMC3340539](#)
- Karagkouni A, Alevizos M, Theoharides TC. Effect of stress on brain inflammation and multiple sclerosis. **Autoimmun Rev.** 2013; 12(10):947-53. PMID: 23537508

3. ***Mast cells and objective biomarkers in autism spectrum disorders.***

- Angelidou A, Francis K, Vasiadi M, Alysandratos KD, Zhang B, Theoharides A, Lykouras L, Sideri K, Kalogeromitros D, Theoharides TC. Neurotensin is increased in serum of young children with autistic disorder. **J Neuroinflammation.** 2010; 7:48. PMID: 20731814; [PMCID: PMC2936302](#)
- Tsilioni I, Dodman N, Petra AI, Taliou A, Francis K, Moon-Fanelli A, Shuster L, Theoharides TC. Elevated serum neurotensin and CRH levels in children with autistic spectrum disorders and tail-chasing bull terriers with a phenotype similar to autism. **Translational Psychiatry.** 2014; 4:e466. PMID: 25313509
- Tsilioni I, Taliou A, Francis K, Theoharides TC. Children with autism spectrum disorders, who improved with a luteolin-containing dietary formulation, show reduced serum levels of TNF and IL-6. **Translational Psychiatry.** 2015 Sep 29;5:e647
- Theoharides TC, Stewart JM, Panagiotidou S, Melamed I. Mast cells, brain inflammation and autism. **Eur J Pharmacol.** 2015 May 1. [Epub ahead of print]. PMID: 25941080
- Theoharides TC, Tsilioni I, Patel AB, Doyle R. Atopic diseases and inflammation of the brain in autism spectrum disorders. **Translational Psychiatry.** 2016, in press.

4. ***The natural flavonoids quercetin and luteolin have potent anti-oxidant and anti-inflammatory actions, while also inhibiting activation of keratinocytes, mast cells, microglia, and T-cells.***

- Middleton E Jr, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. **Pharmacol Rev.** 2000; 52(4):673-751. PMID: 11121513
- Kempuraj D, Tagen M, Iliopoulou BP, Clemons A, Vasiadi M, Boucher W, House M, Wolfberg A, Theoharides TC. Luteolin inhibits myelin basic protein-induced human mast cell activation and

mast cell-dependent stimulation of Jurkat T cells. *Br J Pharmacol*. 2008; 155(7):1076-84. PMID: 15912140; PMCID: 2597265

- Kandere-Grzybowska K, Kempuraj D, Cao J, Cetrulo CL, Theoharides TC. Regulation of IL-1 induced selective release of IL-6 from human mast cells and inhibition by quercetin. *Br J Pharmacol*. 2006 May;148(2):208-15. PMID:16532021
- Weng Z, Patel AB, Panagiotidou S, Theoharides TC. The novel flavone tetramethoxyluteolin is a potent inhibitor of human mast cells. *J Allergy Clin Immunol*. 2014; 135(4):1044-1052.e5. PMID: 25498791
- Theoharides TC, Stewart JM, Hatziagelaki E, Kolaitis G. Brain "fog," inflammation and obesity: key aspects of neuropsychiatric disorders improved by luteolin. *Front Neurosci* 2015;9:225. PMID: 26190965

5. Mast cells are involved in inflammatory conditions.

- Theoharides TC and Canellakis ZN. Spermine inhibits induction of ornithine decarboxylase by cAMP but not by dexamethasone in rat hepatoma cells. *Nature* 1975; 255:733-734. PMID: 49027
- Theoharides TC, Zhang B, Kempuraj D, Tagen M, Vasiadi M, Angelidou A, Alysandratos KD, Kalogeromitros D, Asadi S, Stavrianeas N, Peterson E, Leeman S, Conti P. IL-33 augments substance P-induced VEGF secretion from human mast cells and is increased in psoriatic skin. *Proc Natl Acad Sci USA*. 2010; 107(9):4448-53. PMID: 20160089; PMCID: 28401321
- Theoharides TC, Alysandratos KD, Angelidou A, Delivanis DA, Sismanopoulos N, Zhang B, Asadi S, Vasiadi M, Weng Z, Miniati A, Kalogeromitros D. Mast cells and inflammation. *Biochim Biophys Acta*. 2012; 1822(1):21-33. PMID: 21185371; PMCID: PMC3318920
- Theoharides TC. Atopic conditions in search of pathogenesis and therapy. *Clin Ther*. 2013; 35(5):544-7. PMID: 23642292
- Theoharides TC, Valent P, Akin C. Mast cells, mastocytosis and related disorders. *New Engl J Med*. 2015; 373(2):163-72. PMID:26154789

For a full list of publications, see My Bibliography at the following link:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/theoharis.theoharides.1/bibliography/40779374/public/?sort=date&direction=ascending>

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D. Research Support

Ongoing Research Support

Pfizer #W1194875

Duration 1/1/15-12/31/16

PI: Theoharides

Effect of inflammasome in psoriasis

Completed Research Support

National Psoriasis Foundation Translational Award

Duration: 6/1/13-5/31/15

PI: Theoharides

The role of the novel mTOR pathway in psoriasis and the effect of methoxyluteolin

Autism Research Institute

Duration: 7/1/14-6/30/15

PI: Theoharides

Serum levels of CRH, neurotensin and mitochondrial DNA in children with autism

1 R01 NS071361-05

Duration: 7/1/10-6/30/15

PI: Theoharides

Brain mast cells and chronic fatigue syndrome

1 R01 NS066205-04

Duration: 7/1/10-6/30/15

MPI: Veves and LoGerfo; Role: Subcontract

Role of neuropeptides in diabetic foot problems

2 R01 AR47652-11

Duration: 9/1/07-8/31/13

PI: Theoharides

Stress induces skin mast cell activation and vasodilation